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| EXAMINER |
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BROOKS, KRISTIE LATRICE

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| ART UNIT | PAPER NUMBER |
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1616

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/519,008 | BELANOFF, JOSEPH K. | |
| | Examiner | Art Unit | |
| | Kristie L. Brooks | 1616 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 5-7 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 8-19 is/are rejected.
- 7) ☒ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-4 and 8-19 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>6/4/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application

1. Claims 1-19 are pending.
2. The elected claims 1-4 and 8-19 are presented for examination and the non-elected claims 5-7 have been withdrawn from consideration.
3. New grounds of rejections.
4. This action is non-final.

Withdrawn Rejections/Objections

Specification

5. The abstract of the disclosure was objected to because it was not descriptive enough of the invention and the abstract should be between 50-150 words in length. The Examiner has withdrawn the objection in light of Applicants amendment filed on October 3, 2007.

6. Claim 8 was objected to because of the following informalities: a period is missing at the end of the claim. The Examiner notes Applicants submission of a amended claim set that more clearly identifies the period and as such the Examiner has withdrawn the objection.

7. Claim 12 was objected to because of the following informalities: a typographical error in the spelling of "ribavarin" should be corrected to -- ribavirin--. The Examiner has withdrawn the objection in light of Applicants amendment filed on October 3, 2007.

8. The rejection of claims 1-4, and 13-19 under 35 U.S.C. 102(b) as being anticipated by Schatzberg et al. (US 6,150, 349) is withdrawn in light of Applicants amendment filed on October 3, 2007.

9. The rejection of claims 20-22 under 35 U.S.C. 102(a,e) as being anticipated by Rubinfeld (US Pub No. 2002/0111362)) is withdrawn in light of Applicants cancellation of claims 20-22 in the amendment filed on October 3, 2007.

10. The rejection of claims 1-4, 8-12, and 16-17 under 35 U.S.C. 103(a) as being unpatentable over Korant (US 6,649,644) in view of Bozikas et al. (*A interferon- α -induced psychotic disorder in a patient with chronic hepatitis C*, European Psychiatry, vol. 16, pages 136-137, 2001) is withdrawn in light of Applicants amendment filed on October 3, 2007.

New Grounds of Rejections

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. Claims 1-4, 8-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schatzberg et al. (US 6,150, 349) in view of Ademmer et al. (Suicidal Ideation with IFN- α and Ribavirin in a Patient with Hepatitis C, *Psychosomatics* 42:4, 365-367, 2001).

Applicant claims a method of ameliorating the symptoms of psychosis associated with interferon- α therapy in a patient comprising administering to the patient having received interferon- α therapy and suffering from psychosis associated with the interferon- α therapy, an amount of a glucocorticoid receptor antagonist effective to ameliorate the symptoms of psychosis in the patient, with the proviso that the patient is not otherwise in need of treatment with a glucocorticoid receptor antagonist.

Determination of the scope and content of the prior art
(MPEP 2141.01)

Schatzberg et al. teach a method of ameliorating psychosis to patient in need thereof, including the psychotic component of pathologies or conditions with psychotic symptoms (see the entire article, especially column 1 lines 19-21). The term "psychosis" can refer to a psychiatric condition or symptom associated with a medical condition, a disease state or other conditions such as a side effect of a medication or side effect of drug abuse (see the entire article, especially column 6 lines 25-32). The method of ameliorating psychosis, particularly psychosis associated with major depression, comprises administering an effective amount of a glucocorticoid receptor antagonist where the glucocorticoid receptor antagonist used in the methods can comprise a steroidal skeleton with at least one phenyl-containing moiety in the 11-beta position of the steroidal skeleton where the phenyl-containing moiety in the 11-beta position of the steroidal skeleton can be a dimethylaminophenyl moiety and the glucocorticoid receptor antagonist can comprise mifepristone (RU486), 11- β -(4-dimethyl-aminoethoxyphenyl)-17 α -propynyl- 17 β -hydroxy-4,9-estradien-3-one(RU009), and 17 β -hydrox-17 α -19-(4-methyl-phenyl)androsta-4,9 (11)-dien-3-one (RU044) (see the entire article, especially column 3 lines 46-63; column 10 lines 7-21). The glucocorticoid antagonist can be administered by oral administration, topical administration, aerosol formulations, where the dosage of mifepristone can be about 2-

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30mg per kg of body weight per day (see the entire article, especially column 20 lines 25-45; column 21 lines 56-68).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Schatzberg et al. do not teach ameliorating the symptoms of psychosis associated with a patient having received interferon- α therapy and is suffering from psychosis associated with interferon- α therapy by administering a glucocorticoid receptor antagonist. Schatzberg et al. do not teach administering the glucocorticoid receptor antagonist in combination with interferon- α and a second therapeutic agent. These deficiencies are cured by the teaching of Ademmer et al.

Ademmer et al. teach the state of the art treatment for hepatitis C virus (HCV) is the combination therapy with interferon alpha (IFN- α) and ribavirin (see the entire article, especially the first paragraph in the first column). One of the most serious side effects of the IFN- α treatment is the development of psychiatric symptoms, particularly depression and suicidal ideation (see the entire article, especially the first paragraph in the first column on page 365). In a case report, a 55 year old, Mr. A with a chronic active infection of HCV, started on treatment with IFN- α and ribavirin (see the entire article, especially the first paragraph under the Case Report). Immediately after starting therapy Mr. A appeared to be depressed and became progressively isolated (see the entire article, especially the second paragraph under the Case Report in column 2 on

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page 365). After four months of receiving treatment for his hepatitis C infection, Mr. A was admitted to a psychosomatic ward where he met criteria for major depression (see the entire article, especially the last sentence in the second paragraph under the Case Report and the third paragraph under the Case Report on page 366).

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to ameliorate the symptoms of psychosis associated with a patient having received interferon- α therapy and is suffering from psychosis associated with interferon- α therapy by administering a glucocorticoid receptor antagonist and to further administer the glucocorticoid receptor antagonist in combination with interferon- α and a second therapeutic agent.

One of ordinary skill in the art would have been motivated to do this Schatzberg et al. suggests the use of a glucocorticoid receptor antagonist for treating the symptoms of psychosis (e.g. major depression) caused by the side effects of a medication. Although Schatzberg et al. do not teach the specific medication for which side effects will occur, it is well known in the art that major side effects are associated with receiving IFN- α drug treatment which includes the development of psychiatric

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symptoms, such as major depression as taught by Ademmer et al. Thus, it would have been obvious to one of ordinary skill in the art because patients receiving IFN- α treatment are at risk for developing psychiatric symptoms and the glucocorticoid receptor antagonist is effective at treating psychosis caused by side effects of a medication. Furthermore, although Schatzberg et al. do not teach using the glucocorticoid receptor antagonist concomitantly with the interferon- α and ribavirin, it would have been obvious to one of ordinary skill in the art because it provides the patient protection against developing psychosis throughout the IFN- α treatment. Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made because the prior art is fairly suggestive of the claimed invention.

Response to Arguments

Although Schatzberg et al. no longer anticipates the instant claims, Schatzberg et al. has been maintained as a primary reference in the above rejection; therefor the merits of Schatzberg et al. will be addressed.

Applicant argues that psychosis is a symptom, not a disease. Applicant argues that Schatzberg et al. teach a method of ameliorating psychosis associated with psychotic major depression and that Schatzberg et al. do not disclose the treatment of a patient suffering from psychosis resulting from the treatment with interferon- α therapy.

It is noted that the preferred embodiment in the disclosure of Schatzberg et al. is directed to treating psychosis associated with psychotic major depression. However, the prior art also defines "psychosis" to not only include psychiatric or medical conditions but also to refer to the side effects of a medication. Thus, Schatzberg et al. is capable of treating the psychotic major depression as an illness itself or as a symptom resulting from the medication.

13. Claims 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schatzberg et al. (US 6,150, 349) in view of Ademmer et al. (Suicidal Ideation with IFN- α and Ribavirin in a Patient with Hepatitis C, *Psychosomatics* 42:4, 365-367, 2001) further in view of Dieterich (Treatment of Hepatitis C and Anemia in Human Immunodeficiency Virus-Infected Patients, *The Journal of Infectious Diseases*, 185(Suppl 2):S128-37, 2002)

Applicant claims a method of ameliorating the symptoms of psychosis associated with interferon- α therapy in a patient comprising administering to the patient having received interferon- α therapy and suffering from psychosis associated with the interferon- α therapy, an amount of a glucocorticoid receptor antagonist effective to ameliorate the symptoms of psychosis in the patient, with the proviso that the patient is not otherwise in need of treatment with a glucocorticoid receptor antagonist.

Determination of the scope and content of the prior art

(MPEP 2141.01)

The disclosure of Schatzberg et al. is set forth above. Specifically, Schatzberg et al. teach a method of ameliorating psychosis to patient in need thereof comprising administering an effective amount of a glucocorticoid receptor antagonist.

The disclosure of Ademmer et al. is set forth above. Specifically Ademmer et al. teach the state of the art treatment for hepatitis C virus (HCV) is the combination therapy with interferon alpha (IFN- α) and ribavirin. And that one of the most serious side effects of the IFN- α treatment is the development of psychiatric symptoms, particularly depression and suicide ideation.

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Schatzberg et al. and Ademmer do not teach ameliorating the symptoms of psychosis associated with a patient having received interferon- α therapy and is suffering from leukemia, HIV, Human T-Cell Lymphotropic virus or cancer or has a history of substance abuse. This deficiency is cured by the teachings of Dieterich.

Dieterich teaches that co-infection of hepatitis C virus (HCV) and human immunodeficiency virus (HIV) is common, especially among intravenous drug abusers (see the entire article, especially the second paragraph under the introduction). Patients receiving IFN- α and ribavirin therapy can experience side effects such as influenza-like

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syndrome and other side effects that persist or increase with continued treatment such as neuropsychiatric effects including depression, anxiety, personality change etc (see the entire article, especially page S134, the third paragraph in the first column and the second and third paragraph in the second column).

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to ameliorate the symptoms of psychosis associated with a patient having received interferon- α therapy and is suffering HIV and has a history of substance abuse comprising administering a glucocorticoid receptor antagonist.

One of ordinary skill in the art would have been motivated to do this because Dieterich suggest that it is common for a patient to be co-infected with HCV and HIV, especially among intravenous drug users. It is also known that co-infected patients treated with interferon- α and ribavirin can develop neuropsychiatric effects such as depression. Thus, it would have been obvious to one of ordinary skill in the art to treat a co-infected patient who has a history of substance abuse receiving IFN- α treatment with a glucocorticoid receptor antagonist because are they are still prone to developing side caused by side effects of the medication (i.e. IFN- α treatment). Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art

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at the time the invention was made because the prior art is fairly suggestive of the claimed invention.

Conclusion

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kristie L. Brooks whose telephone number is (571) 272-9072. The examiner can normally be reached on M-F 8:30am-6:00pm Est..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Sharmila Landau
Primary Examiner
Art Unit 1616

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. Claims 1-4, 8-12, and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Korant (US 6,649,644) in view of Bozikas et al. (*A interferon- α -induced psychotic disorder in a patient with chronic hepatitis C*, European Psychiatry, vol. 16, pages 136-137, 2001).

The claims are drawn to a method of ameliorating the symptoms of psychosis associated with interferon- α therapy in a patient comprising administering an amount of a glucocorticoid receptor antagonist effective to ameliorate the symptoms of psychosis

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in the patient, with the proviso that the patient is not otherwise in need of treatment with a glucocorticoid receptor antagonist.

Korant teaches a method of treating chronic viral infections, such as hepatitis B virus and hepatitis C virus comprising administering to a mammal a therapeutically effective amount of a combination (i.e. concurrently, sequentially or at the same time) of: (i) at least one cytotoxic agent (e.g. cyproterone acetate (which is also a glucocorticoid receptor antagonist)) and (ii) at least one antiviral agent such as interferon alpha, and interferon alpha plus virazole (also known as ribavirin) (see the entire article, especially the abstract; column 2 lines 59-67; column 3 lines 25-33 and lines 63-67; column 4 lines 1-13, lines 30-40 and lines 44-48)

Korant does not expressly teach ameliorating the symptoms of psychosis associated with interferon- α therapy.

Bozikas et al. teaches a case of induced INF- α 2b psychotic symptoms in a man with chronic hepatitis C one day after the administration of his standard dose of INF- α 2b (see the entire articles, especially the first and second paragraph).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to ameliorate the symptoms of psychosis associated with interferon- α therapy comprising administering a glucocorticoid receptor antagonist,

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interferon- α and ribavirin. One of ordinary skill in the art would have been motivated to do this because Korant suggests the combination of a cytotoxic agent such as cyproterone acetate (i.e. a glucocorticoid receptor antagonist) and at least one antiviral agent such as interferon alpha plus virazole (also known as ribavirin) in the treatment of viral infections such as both hepatitis B and hepatitis C. It is well known in the art that neuropsychiatric side effects, including psychosis, are associated with interferon- α treatments in patients with chronic hepatitis C as suggested by Bozikas et al. and it would be obvious to ameliorating the symptoms of psychosis as claimed in the instant invention because the method taught by Bozikas et al. is composed of the same ingredients.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of

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ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kristie L. Brooks whose telephone number is (571) 272-9072. The examiner can normally be reached on M-F 8:00am-5:30pm Est..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on (571) 272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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KB

A handwritten signature in black ink, appearing to read "Johann R. Richter", with a long horizontal stroke extending to the right.

Johann R. Richter
Supervisory Examiner
Technology Center 1600